·专家共识·

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中国髋、膝关节置换术围术期抗纤溶药序贯抗凝血药应用方案的专家共识*

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髋、膝关节置换术常可伴随大量失血。根据文献报道，髋、膝关节置换术围术期总失血量多在1000 ml以上，输血率高达30%~60%[1,2]。大量失血可增加患者的围术期风险和经济负担[3]。髋、膝关节置换术围术期失血除手术切口直接出血外，由手术创伤引起的纤溶反应增强所致的失血约占总失血量的60%[4]。而且，膝关节置换术中应用止血带引起的组织缺血再灌注损伤可进一步增强纤溶反应[5]，增加出血量。

氨甲环酸（tranexamic acid，TXA）是一种抗纤溶药，其与纤溶酶原的赖氨酸结合位点具有高亲和性，可封闭纤溶酶原的赖氨酸结合位点，使纤溶酶原失去与纤维蛋白结合的能力，导致纤溶活性降低，从而发挥止血作用[6]。目前，大量研究均已证实氨甲环酸能有效减少髋、膝关节置换术围术期的失血量并降低输血率，且不增加术后静脉血栓栓塞症的发生风险[5-8]。

髋、膝关节置换术患者是静脉血栓栓塞症的高发人群，应用抗凝血药物能有效降低静脉血栓栓塞症的发生率。为了在髋、膝关节置换术围术期更好地平衡抗纤溶药与抗凝血药的应用，既可减少患者的出血量、降低输血率，又不增加患者发生静脉血栓栓塞症的风险，保障医疗安全。国家卫生计生委公益性行业科研专项《关节置换术安全性与效果评价》项目组（项目编号：201302007）和《中华骨与关节外科杂志》编辑部邀请国内专家，复习国内外27篇meta分析和260多篇论著，结合项目组26家大型医院数据库和50家推广医院数据库共13300例髋、膝关节置换术病例中8426例氨甲环酸应用经验以及全国12场氨甲环酸临床应用区域会议征求意见结果，遵循循证医学原则，达成髋、膝关节置换术围术期抗纤溶药序贯抗凝血药应用的专家共识，供广大骨科医师在临床工作中参考应用。但在应用氨甲环酸前应结合患者的全身情况，参照氨甲环酸药物说明书或《中国药典》，遇有不良反应及时处理。

1 髋关节置换术围术期的氨甲环酸应用

1.1 静脉应用

11篇meta分析[8-18]及19篇前瞻性随机对照研究[19-37]报道氨甲环酸给药方式主要为单次静脉滴注或二次间隔静脉滴注，二次给药间隔时间为3 h。单次给药剂量为15~20 mg/kg或总量1 g；二次间隔给药剂量为每次10~20 mg/kg或每次总量1 g。

推荐：①单次给药法：髋关节置换术切开皮肤前5~10 min氨甲环酸15~20 mg/kg或总量1 g静脉滴注完毕；②二次间隔给药法：首次给药同单次给药法，3 h后根据引流情况再次给药，剂量同前。

1.2 局部应用

研究表明，氨甲环酸局部应用能够提高局部药物浓度，减少全身吸收[38]。1篇meta分析[39]及4篇前瞻性随机对照研究[38,40-42]报道氨甲环酸2~3 g局部应用可以有效减少出血、降低输血率。目前，有关氨甲环酸的局部应用尚无统一标准，特别是对于术后是否放置引流管及引流管夹闭后何时开放仍存在争议，各报道中术后引流管夹闭时间为30 min~2 h不等。因此，氨甲环酸在髋关节置换术中局部应用的具体方法及术后引流管夹闭时间有待进一步研究。

推荐：氨甲环酸在髋关节置换术中局部应用的推荐剂量为2~3 g。

1.3 静脉和局部联合应用

研究报道，氨甲环酸在髋关节置换术围术期静脉滴注联合局部应用相比单纯静脉滴注或局部应用能更有效减少出血、降低输血率[43]。具体方法为髋关

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节置换术切开皮肤前5~10 min氨甲环酸15~20 mg/kg静脉滴注完毕，同时关闭切口前以总量1~2 g氨甲环酸局部应用。

推荐：髋关节置换术切开皮肤前5~10 min氨甲环酸15~20 mg/kg静脉滴注完毕，同时关闭切口前氨甲环酸1~2 g局部应用。

2 膝关节置换术围术期的氨甲环酸应用

2.1 静脉应用

13篇meta分析[7,9,44-54]及16篇前瞻随机对照研究[5,19,55-68]报道，氨甲环酸给药方式主要为单次静脉滴注或二次间隔静脉滴注，二次给药间隔为3 h。单次给药时间应在手术开始前（不用止血带者）或松止血带前5~10 min，剂量为10~20 mg/kg或总量1 g；二次给药时间为首次给药后3 h再次给药，剂量为每次10~20 mg/kg或每次总量1 g。

推荐：①单次给药法：膝关节置换术切开皮肤前（不用止血带者）或松止血带前5~10 min氨甲环酸10~20 mg/kg或1 g静脉滴注完毕；②二次间隔给药法：首次给药同单次给药法，3 h后根据引流情况再次给药，剂量相同。

2.2 局部应用

4篇meta分析[69-72]及12篇前瞻随机对照研究[73-84]报道氨甲环酸局部应用的最低有效剂量≥2 g[70]、最低有效浓度≥20 mg/ml[71]，大剂量（≥2 g）和高浓度（≥20 mg/ml）氨甲环酸局部应用能有效减少膝关节置换术围术期出血、降低输血率。局部应用方法为关闭切口前关节腔灌注，或关闭切口后通过引流管逆行注入，或通过注射器关节腔内注射。各报道中术后引流管夹闭时间为30 min~2 h不等，仍存在争议，有待进一步研究。

推荐：氨甲环酸在膝关节置换术中的局部应用应在关闭切口前后，局部应用的剂量≥2 g或浓度≥20 mg/ml。

2.3 静脉和局部联合应用

联合给药方法为松开止血带5~10 min前氨甲环酸15~20 mg/kg或1 g静脉滴注，同时关闭切口前氨甲环酸1~2 g局部注入。联合用药能有效减少膝关节置换术围术期出血、降低输血率[85]。

推荐：膝关节置换术切开皮肤前（不用止血带者）或松止血带前5~10 min氨甲环酸15~20 mg/kg或1 g静脉滴注完毕，同时关闭切口前氨甲环酸1~2 g局部应用。

3 髋、膝关节置换术围术期抗纤溶药序贯抗凝血药应用

髋、膝关节置换术围术期应用抗纤溶药氨甲环酸后序贯应用抗凝血药，既能减少出血，又不增加静脉血栓栓塞症发生风险。氨甲环酸的止血效果与其应用剂量和应用次数有关，但随着剂量或次数的增加，静脉血栓栓塞症的发生风险也可能增大。理论上认为，抗凝血药物在术后应用越早、持续时间越长，患者发生静脉血栓栓塞症的风险越小，但发生出血的风险增大。为了达到抗纤溶药和抗凝血药的平衡，应在髋、膝关节置换术围术期应用氨甲环酸6 h后根据引流量的变化，选择抗凝血药应用时间。大部分患者术后6~12 h内伤口出血趋于停止，如引流管无明显出血或引流管血清已分离则表明伤口出血趋于停止，应在12 h内应用抗凝血药；若个别患者术后12 h仍有明显出血，可延后应用抗凝血药。

髋、膝关节置换术后抗凝血药物预防持续时间应根据《中国骨科大手术静脉血栓栓塞症预防指南》，推荐预防时间最短为10 d，可延长至11~35 d[86]。在应用时应注意抗凝血药物的有效性和安全性，当患者出现凝血功能异常或出血事件时，应综合评价出血与血栓的风险，及时调整药物剂量或停用。

本共识制定专家和项目组专家共54人，各位专家在共识制定过程中贡献了自己的宝贵经验和建议，才使得共识达到了更高的学术水平和应用价值，特向各位专家致以衷心地感谢！

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